Original Research Paper

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EFFICACY OF ONDANSETRON IN THE CONTROL OF NAUSEA AND VOMITING DURING AND AFTER CAESAREAN SECTION UNDER SPINAL ANAESTHESIA- A RANDOMIZED DOUBLE BLINDED CONTROLLED TRIAL

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ABSTRACT

Background; Ondansetron has been successfully used to control emesis in various clinical situations mainly during chemotherapy, radiotherapy and operative and postoperative conditions. Aim of this study is to evaluate the efficacy and safety of ondansetron in the control of nausea, retching and vomiting during and after caesarean section under spinal anaesthesia.

Materials and Methods; This randomized controlled trial conducted among 50 pregnant patients were scheduled to undergo elective caesarean section belonging to ASA physical status 1 and 2 in the age of 20-40 years. Group I (study group) received ondansetron 4 mg intravenously and Group II patient (control group) received placebo injection or normal saline intravenously after delivery of the baby and umbilical cord clamping.

Results; The age,height,weight,gravidity and initial mean BP were similar in both groups. There is statistically significant difference among the placebo group and ondansetron group in control of nausea and vomiting during and after caesarean section under spinal anaesthesia as detected by chi square test by which the probability was <0.01.

Conclusion; In this study, it is inferred that intraoperative intravenous injection of ondansetron 4 mg is highly efficacious in reducing the incidence of vomiting and the severity of nausea during and after caesarean section under spinal anaesthesia and also very safe with minimal side effects

KEYWORDS : Ondansetron, Post operative Nausea, Spinal Anaesthesia.

INTRODUCTION

The first extensive description of postoperative nausea and vomiting was made by john snow in 1848 in his book within 2 years of the demonstration of ether anaesthesia with W.T.G.Morton in 1846.[1]

Although much effort rightly has been placed on providing adequate pain relief after surgery, many physicians continue to view postoperative nausea and vomiting as a minor complication that posses little threat to the patient. In contrast many patients view post operative nausea and vomiting as more debilitating than the surgery itself. This complication is not only unpleasant aesthetically displeasing to patients and their care givers, but, when severe, may also be associated with stress on suture lines, wound dehiscence, bleeding, electrolyte imbalance, dehydration and on rare occasions pulmonary aspiration of gastric contents. Post operative nausea and vomiting delays discharge and results in an increased use of resources which have financial implications. Yet this complication has been called the "big, little problem".[2,3,4]

Most mothers request and receive regional anaesthesia for caesarean section. Nausea and vomiting are important side effects both during and after caesarean section under spinal anaesthesia. They may distress the patient and decrease overall satisfaction with pain relief. Hence, the need to prevent nausea and vomiting during and after the surgery is very important. [5,6]

Postoperative nausea and vomiting lasts for less than 24 hourse and usually most intense in the first two hours. In general, vomiting and retching subside before nausea. The incidence of post operative nausea and vomiting is remarkably constant at 18% to 30% in many large series from around the world but varies between institution. However the incidence of severe vomiting has remained remarkably constant at 0.1% to 0.6% some subsets of patients are at high risk to post operative nausea and vomiting.[7,8]

Most antiemetics used currently have significant adverse effects such as sedations, dry mouth, dysphoria, extrapyramidal symtoms etc..,

Ondansetron, a selective 5-hydroxy tryptamine – 3 receptor antagonist is devoid of significant adverse effects and highly cost effective. It has been successfully used to control emesis in various clinical situations mainly during chemotherapy, radiotherapy and operative and postoperative conditions.[9,10] Intra operative administration of ondansetron, single dose, during caesarean section significantly reduces the incidence of vomiting and the severity of nausea.

Ondansetron was synthesized in 1983. It was approved by FDA in January 1991 and marketed in February 1991.it is 5 HT3 receptor antagonist. It act at the 5 HT3 receptor present both peripherally on the vagus nerve terminals and centrally in chemoreceptor trigger zone. oral bioavailability is approximately 60% and food increase its bioavailability. Peak plasma concentration is reached 1.5 hours after oral administration. About 40% of the drug is removed from the systemic circulation by first pass metabolism. Ondansetron hydrochloride dehydrate an isotonic solution containing 2mg/ml. it can be given intravenously or intramuscularly. When given intravenously it should be given as an infusion or by slow IV injection over 2-5 min.[11,12]

Post Operative Nausea and vomiting:

It is used in the prophylaxis of postoperative nausea and vomiting in the dose of 8 mg three times a day orally or 4 mg intravenously or intramuscularly before induction. The dose is 0.1-0.15 mg/kg in children. The ideal dose in adults weighing more than 40 kg is 4mg IV.[13,14,15]

CONTRAINDICATIONS : hypersensitivity to any component of the preparation.

ADVERSE EFFECTS

1. Constipation
2. Increase hepatic transaminase enzymes
3. Headache and rarely, extra pyramidal reactions
4. Cardiovascular effects like tachycardia, bradycardia, angina, hypotension, syncope and second degree heart block have been reported rarely.
5. Transient blurring of vision and dizziness following intravenous infusion
6. A sensation of flushing or warmth in the head and epigastrium
7. Hypokalemia and grandma seizures
8. Musculoskeletal pain and shivers[15]

AIM OF THE STUDY

1. To evaluate the efficacy of single dose of ondansetron 4 mg in the control of nausea, retching and vomiting during and after caesarean section under spinal anaesthesia.
2. To evaluate the safety of the drug by studying the incidence of side effects.

MATERIALS AND METHODS;

This was a randomized, double blind, placebo controlled study conducted at the Government Theni Medical College,Theni. A total of 50 patients who were scheduled to undergo elective caesarean section were selected for the study. To be included in the study, these women were at full – term, 20-40 years of age ASA status 1 or 2, without fetal distress, and able to understand and sign the informed consent form.

Since transmission of ondansetron across the human placenta to the fetus and its effect on the neonate are still unknown, the drug was administered after delivery and Umbilical cord clamping.

Exclusion Criteria;
Since the secretion of ondansetron into colostrums / milk is still undertermined, women who have planned to breast feed were excluded. Exclusion criteria also included significant medical problems such as cardiac, Gastrointestinal, hepatic, renal or known psychiatric disease, pregnancy induced hypertension, history of motion sickness, previous of post operative nausea and vomiting.

Informed consent was obtained from all the patients.

Method of study;
The patients were randomized and divided into two groups each containing 25 patients to receive either ondansetron 4 mg intravenously or placebo injection or normal saline intravenously after delivery of the baby and umbilical cord clamping. The injections were loaded by an anaesthesiologist who was not involved in the assessment of the patients.

Preoperative Visit was done to reduce the anxiety of the patients. No premedication was given to any of the patient.

Anaesthetic technique : Intrathecal injection of 1.8-2 ml (8-10mg) of hyperbaric bupivacaine 0.5% was used in all cases without any adjuvant like opiods which may initiate nausea and vomiting. Also the patient would be excluded if any opioid or an anaesthetic was required to control intra operative pain. After induction of spinal anaesthesia with the patient in lateral position. The uterus was tilted to the left, oxygen was administered by plastic face mask and pulse oximeter placed. Vital signs (heart rate, non invasive BP, respiratory rate) were recorded before anaesthesia and every 5 minutes there after. The preoperative values for the vital signs were the mean of three readings within 10 minutes of the spinal block. The sensory level as determined by pin prick was measured every 5 min.

One litre of lactated ringer solution was administered within 20 min of the spinal block and another litre continued during surgery. More fluid was administered when required depending on the cardiovascular stability and clinical estimation of blood loss. To prevent hypotension ephedrine hydrochloride was given at dose of 6-12 mg whenever necessary.

Hypotension was defined as decrease of the mean arterial blood pressure by 20%. When it occurred it was treated promptly by additional fluids and intravenous increments of ephedrine.

In all patients the uterus was exteriorized during surgery. After delivery and umbilical cord clamping, 2ml containing either ondansetron 4mg or 0.9% saline were injected intravenously. The study period continued for 24 hours. Following injectate to cover the period in the operating theatre, the recovery room and the immediate postoperative period. Before and at 15 min intervals following drug injection, the presence or absence and severity of nausea were recorded on a verbal analogue score extending from none = 0 to maximum nausea = 10.

The severity and frequency of vomiting, including retching were recorded before and after the injectate.

Post operative monitoring : the patients was assessed for nausea and vomiting at the time of recovery and then at 1 hour, 4 hour and 24 hours. Complaints of nausea and vomiting between the assessment period were recorded. All the patients were asked about other complaints like headache, dizziness, constipation etc..

Pain relief was given postoperatively with Inj Diclofenac IM for all patients in both placebo and study group. Injection metoclopramide 10 mg iv was given as a rescue antiemetic for patients who had vomiting.

The collected data was analysed with SPSS 16.0 version. Percentage analysis were used for categorical data and for continuous variables mean and SD were used. Chi square and student t test were used to find the significance. P value <0.01 was considered significant.

OBSERVATIN AND RESULTS

A total of 50 patients were taken for study. They were divided into two groups to receive either normal saline as placeho or ondansetron. There were no significant differences between the two groups in terms of age, weight or other parameters. The total duration of surgery was 45-60 minutes.

Table-1 SUMMARY STATICTICS OF MATERNAL CHARACTERISTICS MEAN (SD)

	Placebo (n=25)	Ondansetron (n=25)
AGE (yrs)	24.24 (2.4)	24.12 (3.54)
WEIGHT (kg)	59.52 (3.74)	60 (4.18)
GRAVIDITY	GI (7/25) 28% Multi (18 / 25) 72%	GI (9/25) 36% Multi (16/25) 64%
INITIAL MEAN BP (mm Hg)	92.17 (4.59)	92.8(5.08)

The ranges of age, weight, Gravidity and initial mean BP were similar and statistically in significant.

Table-2 SUMMARY STATISTICS OF SURGICAL VARIABLES MEAN

	Placebo (n=25)	Ondansetron (n=25)
Surgical time (min)	42.2	45
Bupivacaine does. In. mg	8.96	9.28
Final sensory level	T4	T4
Incidence of nausea and vomiting before injection	0	0
Hypotension incidence	12%	8%
Ephedrine dose in mg	12	12

The incidence of nausea, retching and vomiting were observed in the 0-1 hrs, 1-4 hours, 4-24 hours the observation are as follows.

Table-3 Number of patients with nausea.

Injection	0-1 hours	1-4 hours	4 – 24 hours
Placebo	9	3	1
Ondansetron	1	1	0

Prior to placebo or drug administration, the incidence of nausea and vomiting did not differ between the groups. Also, the time of occurrence of nausea, retching and vomiting in regional anaesthesia for caesarean section, in contrast to general anaesthesia, is mainly intraoperative and in immediate post operative period. (in the 0-1 hr period 9 patients in the placebo group and 1 patient in the ondansetron group experienced nausea. In the 1-4 hours period, 3 patients in the placebo group and 1 patient in the ondasetron group experienced nausea) 1 patients experienced nausea in the 4-24 hours period in the placebo group.

Table-4 Number of patients with retching

Injection	0-1 hours	1-4 hours	4 – 24 hours
Placebo	7	3	0
Ondansetron	1	0	0

7 patients had retching in the placebo group in the first hour as compared to 1 patient in the ondansetron group. In the immediate post operative period of 1-4 hours. 3 patients had retching in the placebo group and none in the ondansetron group. In the 4-24 hours period. None of the patient in both the group had retching.

Table-5 Number of patients with vomiting

Injection	0-1 hours	1-4 hours	4 – 24 hours
Placebo	6	2	0
Ondansetron	0	0	0

No patients had vomiting four hours after surgery 6 patients post operative period. The incidence in the ondansetron group is none in the 24 hours period. Rescue antiemetic injection metoclopramide 10 mg was given to patients who had vomiting.

Table-6 24 hours occurrence of nausea, retching vomiting

	Placebo	Ondansetron
Nausea	13	2
Retching	10	1
Vomiting	8	0

Table shows the overall occurance of nausea, retching and vomiting in 24 hours observation period. There is statistically significant difference among the placebo group and ondansetron group in control of nausea and vomiting during and after caesarean section under spinal

anaesthesia as detected by chi square test by which the probability was <0.01 which means that there is significant difference between the two groups.

The study results show that the

1. Incidence of nausea was 52% in the placebo group and 8% in the ondansetron group.
2. Incidence of retching was 40% in the placebo group and 4% in the ondansetron group.
3. Incidence of vomiting was 32% in the placebo group and 0% in the ondansetron group.

In the 24 hours observation period the overall incidence of nausea, retching and vomiting was 52% in the placebo group and 8% in the ondansetron group. A statistically significant difference exist between the two group as tested and proved by chi square test by which the 'p' value is < 0.01.

Thus a single dose of intraoperative intravenous administration of ondansetron 4mg, after clamping of the cord, during caesarean section reduces the incidence of nausea retching and vomiting by 44%.

DISCUSSION

Nausea, retching, and vomiting are a common and distressing problem which are not only unpleasant and aesthetically displeasing to the patient and their care givers, but, when severe, may also be associated with other potentially dangerous and even lethal complication, such as pulmonary aspiration of gastric contents.

Intra operative nausea, retching, and vomiting during caesarean section under regional anaesthesia can be problematic and effort should be made to control them.

Chestnut DH, Owen CL et studied the incidence of nausea and vomiting during epidural anaesthesia. They tried drugs like metaclopramide and droperidol and found them to be effective but with some side effects.

Pan PH, Moore CH et al compared the older drugs like droperidol with newer 5HT3 antagonist ondansetron and found it very effective and safe in caesarean section under epidural anaesthesia.

Our study showed ondansetron to be an effective antiemetic drug during the intra – operative and immediate post operative period for prevention and control of nausea, retching and vomiting during and after caesarean section under spinal anaesthesia. This confirms the beneficial effects of ondansetron as reported by Pan and Moore et al in patients undergoing caesarean section under epidural anaesthesia and E.I Abouleish et al study similar to ours on which this study is we have used a smaller dose of ondansetron, 4mg instead of 8mg based on the work of Pearman and Claybon. In our study we have excluded those patient with factors that might influence nausea and vomiting for example opioids, antacids, history of gastro intestinal disease and morbid obesity.

The incidence of emesis in our study is higher than previously published in studies conducted by Kang Y G et al and Santos A Datta. The possible reasons for this difference are the

1. Routine exteriorization of the uterus
2. Use of spinal Vs epidural anaesthesia as reported in other studies.
3. The routine administration of oral antacids in most of them
4. The possibility of racial influence.

The time of occurrence of nausea and vomiting in regional anaesthesia for caesarean section, in contrast to general anaesthesia is mainly intra operative, therefore the timing of anti emetic administration is important. After intravenous injection, the maximum effect of ondansetron is reached in 6-20 min and its half life is 3.5 hours in healthy volunteers as proved in studies conducted by Claybon et al and Fortney JY et al. therefore, it seems preferable to inject the drug before the spinal block. However, since the transmission of ondansetron across the placenta and its effects on fetus and neonate are still unknown. We had to administer the drug after delivery and umbilical cord clamping. Also since it is unclear whether ondansetron is secreted into maternal milk, we had to include only those women who did not breast feed their efforts until 4 hours have elapsed from the surgery.

In conclusion, in women undergoing caesarean section under spinal anaesthesia, the intravenous administration of 4 mg ondansetron significantly reduced the incidence of vomiting and severity of nausea. It was also found to be very safe with only minimal adverse effects.

CONCLUSION

Intraoperative intravenous injection of ondansetron 4 mg is highly efficacious in reducing the incidence of vomiting and the severity of nausea during and after caesarean section under spinal anaesthesia.

It is also very safe with minimal side effects. Thus ondansetron stands out as a near ideal drug for reducing the incidence of nausea and vomiting along with more distressing and potentially lethal complications during caesarean section under spinal anaesthesia.

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